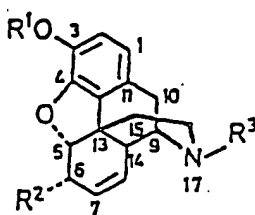




## APPENDIX I

AMENDED CLAIMS WITH AMENDMENTS INDICATED THEREIN  
BY BRACKETS AND UNDERLINING

1. (Amended) Transdermal or transmucosal composition for administering at least one morphine [alkaloids] alkaloid, the composition comprising at least one morphine alkaloid each as the acid addition salt thereof with an organic acid, each said morphine alkaloid being of the following Formula I:



(I)

where  $R^1$  is selected from the group consisting of H,  $C_1$ - to  $C_6$ -alkyl residues[, preferably methyl, ethyl-, propyl, i-propyl,  $C(O)CH_3$ ];  $R^2$  is selected from the group consisting of the monad residues H, OH,  $OC(O)CH_3$ , whereby in this case the fourth valence of the (6)-C atom is occupied by H, or the dyad residues  $=O$ ,  $=CH_2$ ;  $R^3$  is selected from the group consisting of  $-CH_3$ , cyclopropyl, cyclobutyl and allyl; [and where]

[- the bond at C7/C8 may be saturated, or a nitroxyl group may be present at  $N_{17}$ ,]

[characterized in that it contains the morphine alkaloid as an acid addition salt of an] the organic acid [which is] being selected from

- [-] monoesters of C<sub>3</sub>- to C<sub>16</sub>-dicarboxylic acids with monohydric C<sub>1</sub>- to C<sub>4</sub>-alcohols, [especially methanol,]
- [-] C<sub>2</sub>- to C<sub>6</sub>- and C<sub>8</sub>- to C<sub>16</sub>-sulfonic acids,
- [-] substituted benzoic acids, selected from the group consisting of halogen, hydroxy, alkyl, hydroxyalkyl, alkoxyalkyl, [and/or] alkoxy-substituted benzoic acids, [as well as of the] aminosubstituted benzoic acids, [which may optionally be] aminosubstituted benzoic acids alkylated at the N atom,
- [-] substituted or [non-substituted] unsubstituted 5-ring or 6-ring heterocycles comprising at least one N or S atom and having a carboxyl group function[, especially a carboxy, carboxymethyl, carboxyethyl] or [the - optionally] branched [-] or unbranched carboxypropyl or carboxybutyl groups as substituents,
- [-] saturated or unsaturated, [optionally] substituted or unsubstituted, oxo-carboxylic acids having 5 to 10 C atoms,

[-] phenyl-substituted or phenoxy-substituted saturated C<sub>2</sub>- to C<sub>4</sub>-carboxylic acids,

[-] aliphatic, aromatic or heterocyclic C<sub>2</sub>- to C<sub>12</sub>-amino acids, wherein one amino group is substituted with [an - optionally] a substituted or unsubstituted [-] C<sub>2</sub>- to C<sub>6</sub>-alkanoyl group or [an - optionally] a substituted or unsubstituted [-] benzoyl group,

the acid salt having a property of penetrating skin as defined by a flux of at least 2.34  $\mu\text{g}/\text{cm}^2\cdot\text{h}$ .

2. (Amended) Composition according to Claim 1, [characterized in that] wherein the organic acid is selected from aliphatic monoaminomonocarboxylic acids, wherein the amino group is substituted with [a] an unsubstituted C<sub>2</sub>- to C<sub>6</sub>-alkanoyl group[, which may be mono- or polysubstituted with hydroxy] or with a C<sub>2</sub>- to C<sub>6</sub>-alkanoyl group which is monosubstituted or polysubstituted with hydroxy, C<sub>1</sub>- to C<sub>4</sub>-alkoxy- or C<sub>1</sub>- to C<sub>4</sub>-hydroxyalkyl, or wherein the amino group is substituted with [the] an unsubstituted benzoyl residue[, which may be] or with benzoyl residue which is mono- or polysubstituted with C<sub>1</sub>- to C<sub>4</sub>-alkyl, C<sub>1</sub>- to C<sub>4</sub>-alkoxy, C<sub>1</sub>- to C<sub>4</sub>-hydroxyalkyl, halogen, amino or hydroxy.

3. (Amended) Composition according to Claim 2, [characterized in that] wherein the organic acid is selected from aliphatic C<sub>2</sub>- to C<sub>6</sub>-monoaminomonocarboxylic acids, wherein the amino group is substituted with [the] an acetyl group or [the] a benzoyl group.

4. (Amended) Composition according to Claim 1, [characterized in that] wherein the organic acid is selected from:

[-] hydroxy- (C<sub>1</sub>- to C<sub>4</sub>)-alkyl, C<sub>1</sub>- to C<sub>6</sub>-alkoxy-(C<sub>1</sub>- to C<sub>4</sub>)-alkyl-substituted or p- or m-hydroxy-substituted benzoic acids,

[-] monoesters of C<sub>5</sub>- to C<sub>10</sub>-dicarboxylic acids, [especially suberic acid, azelaic acid and sebacic acid,]

[-] C<sub>4</sub>- to C<sub>8</sub>-sulfonic acids[, especially hexanesulfonic acid].

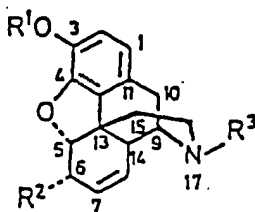
5. (Amended) Composition according to Claim 1, [characterized in that] wherein the acid is selected from C<sub>1</sub>- to C<sub>4</sub>-alkyl-substituted benzoic acids[, preferably C<sub>1</sub>- to C<sub>4</sub>-trialkyl-substituted benzoic acids].

6. (Amended) Composition according to Claim 1, [characterized in that] wherein the organic acid is hexanesulfonic acid, aminobenzoic acid or trimethylbenzoic acid.
7. (Amended) Composition according to Claim 1, [characterized in that] wherein the 5-ring or 6-ring heterocycle is a pyridine-carboxylic acid[, preferably nicotinic acid or lipoic acid].
8. (Amended) Composition according to Claim 1, [characterized in that] wherein the oxocarboxylic acid is a saturated or unsaturated 2-, 4-, 5- or 9--oxocarboxylic acid [which is optionally unsaturated].
9. (Amended) Composition according to Claim 8, [characterized in that] wherein the oxocarboxylic acid is 5-oxopyrrolidine-2-carboxylic acid, levulic acid or oxodec-2-ene acid.
10. (Amended) Composition according to Claim 3, [characterized in that] wherein the organic acid is acetylglycin or hippuric acid.

11. (Amended) Composition according to any one of [the preceding] Claims 1 to 10 and 17 to 25, [characterized in that] wherein the morphine alkaloid is morphine, codeine, heroin, ethylmorphine, levorphanol or hydromorphone.

12. (Amended) Composition according to Claim 1, [characterized in that it comprises] comprising a solution or suspension of the acid addition salt in glycerin, ethylene [glykol] glycol, dimethyl isosorbide, oleic acid and/or dimethyl sulfoxide.

13. (Amended) Acid addition salts of morphine alkaloid and organic acid, said morphine alkaloid having the following Formula I:



(I)

where R<sup>1</sup> is selected from the group consisting of H, C<sub>1</sub>- to C<sub>6</sub>-alkyl residues[, preferably methyl, ethyl-, propyl, i-propyl, C(O)CH<sub>3</sub>]; R<sup>2</sup> is selected from the group consisting of the monad residues H, OH, OC(O)CH<sub>3</sub>, whereby in this case the fourth valence of the (6)-C atom is occupied by H, or the dyad residues =O,

=CH<sub>2</sub>; R<sup>3</sup> is selected from the group consisting of -CH<sub>3</sub>, cyclopropyl, cyclobutyl and allyl; [and where]

[- the bond at C7/C8 may be saturated, or a nitroxyl group may be present at N<sub>17</sub>,]

[characterized in that] the organic acid [is] being selected from

[- monoesters of C<sub>3</sub>- to C<sub>16</sub>-dicarboxylic acids with monohydric C<sub>1</sub>- to C<sub>4</sub>-alcohols, [especially methanol,]

[- C<sub>2</sub>- to C<sub>6</sub>- and C<sub>8</sub>- to C<sub>16</sub>-sulfonic acids,

[- the group of] halogen, p- and m-hydroxy, alkyl, hydroxyalkyl, alkoxyalkyl and/or alkoxy-substituted benzoic acids, [as well as of the] aminosubstituted benzoic acids, [which may optionally be] aminosubstituted benzoic acids alkylated at the N atom,

[- substituted or [non-substituted] unsubstituted 5-ring or 6-ring heterocycles comprising at least one N or S atom and having a carboxyl group function[, especially a carboxy, carboxymethyl, carboxyethyl] or [the - optionally]

branched [-] or unbranched carboxypropyl or carboxybutyl groups as substituents,

[-] saturated or unsaturated, [optionally] substituted or unsubstituted, oxo-carboxylic acids having 5 to 10 C atoms,

[-] phenoxy-substituted saturated C<sub>2</sub>- to C<sub>4</sub>-carboxylic acids,

[-] aliphatic, aromatic or heterocyclic C<sub>2</sub>- to C<sub>12</sub>-amino acids, wherein one amino group is substituted with [an - optionally] a substituted or unsubstituted - C<sub>2</sub>- to C<sub>6</sub>-alkanoyl group or [an - optionally] a substituted [-] or unsubstituted benzoyl group,

the acid salt having a property of penetrating skin as defined by a flux of at least 2.34  $\mu\text{g}/\text{cm}^2\cdot\text{h}$ .

16. (Amended) [Composition according to Claim 1, characterized in that said preparation is a] A lotion, ointment, creme, gel, [or] spray, [an] iontophoretic device, [a] transmucosal therapeutic system or [a] transdermal therapeutic system [(TTS)], [comprising] the transdermal therapeutic system including a backing



layer[,] which [optionally] is [active substance-] permeable or impermeable with respect to the active substance, and a reservoir layer, comprising a composition according to Claim 1.